Notice of Allowability	Application No.	Applicant(s)	
	10/069,056	NUESCH ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *9/27/2004*.

2. ☒ The allowed claim(s) is/are *1,5-9,11 and 19-22*.

3. ☒ The drawings filed on *29 July 2002* are accepted by the Examiner.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Marianne Fuierer on February 14, 2005.

The application has been amended as follows: The claims have been amended as shown on the attached listing of claims.

The following is an examiner's statement of reasons for allowance:

Applicant's amendments and arguments were sufficient to overcome the rejections of record for claims 1, 5, 6, 9. Nuesch et al (Journal of Virology 72:8002-8012, October 1998 and 72:9966-9977, December 1998) are cited as of interest. These references teach that phosphorylation is involved in several NS1 activities, but do not teach or suggest that mutation at different phosphorylation sites can have distinct effects on cytotoxicity and replication/transcription activity, or teach which sites affect which activity.

Claim 1 is amended to clarify that the claim is not limited to the proteins with the full structure of SEQ ID 6, 10, 14, or 18, but is more broadly drawn to a parvovirus NS1 protein with the specified alteration at the specified position. New claim 22 recites the full structure. Claim 8 is amended so that it cannot read upon an intact human person. Claim 10 is cancelled and claim 1 is amended to delete reference to an antibody.

Applicant argues that the different activities of the mutant proteins implies different tertiary structure and there is no indication that the prior art antibodies would recognize the mutant NS1 proteins. However, at least some of the antibodies of Yeung et al are directed at linear epitopes, see Figure 9; these epitopes would be present in the mutant proteins because the mutant and wild-type proteins share the same primary structure in the region recognized by the antibodies. Claims 12 and 13, drawn to therapeutic methods, are cancelled, because the specification gives little or no guidance to development of successful cancer therapies, and cancer treatment using parvovirus NS1 DNA or protein was not routine at the time of the invention.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on M-T and alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

2/14/05

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Claim Listing

1. (Currently amended) A parvovirus NS 1 variant protein having a shifted equilibrium between the DNA replication and transcription activities (a) and the cytotoxicity activity (b), wherein the parvovirus NS 1 variant comprises a mutation S283A ~~(SEQ ID NO. 6)~~; T363A ~~(SEQ ID NO. 10)~~; T394A ~~(SEQ ID NO. 14)~~ or T463A ~~(SEQ ID NO. 18)~~.

2-4. (Cancelled)

5. (Previously presented) A DNA, coding for the parvovirus NS1 variant protein according to claim 1.

6. (Currently amended) The DNA according to claim 5, wherein the DNA comprises a member selected from the group consisting of ~~(a)~~ the DNA of SEQ ID Nos: 4, 8, 12 and 16.

7. (Previously presented) An expression vector, comprising the DNA according to claim 6.

8. (Currently amended) ~~A~~ An isolated host cell, containing the expression vector according to claim 7.

9. (Previously presented) A method of producing the parvovirus NS 1 variant protein according to claim 1, comprising:

(a) transfecting a host cell with a polynucleotide including SEO ID Nos. 4, 8, 12, or 16;

(b) culturing the host cell under conditions sufficient for expression of the narvovirus NS 1 variant protein; and

(c) recovering the parvovirus NS 1 variant protein.

10. (Cancelled)

11. (Currently amended) A Kit comprising at least one member selected from the group consisting of:

(a) a parvovirus NS 1 variant protein comprising a mutation S283A ~~(SEO ID NO 6)~~; T363A ~~(SEO ID NO 10)~~; T394A ~~(SEO ID NO. 14)~~ or T463A ~~(SEO ID NO. 18)~~, and

(b) a DNA of SEO ID Nos. 4, 8, 12 ~~and~~ or 16 , ~~and~~

~~(c) an antibody directed against a parvovirus NS 1 variant Protein of (a);~~

and conventional auxiliary agents, comprising solvents, buffers, carriers markers or controls.

12-18. (Cancelled)

19. (Previously presented) A parvovirus NS 1 variant protein having a shifted equilibrium between the DNA replication and transcription activities (a), and the cytotoxicity activity (b), wherein the parvovirus NS 1 variant protein comprises at least one mutation located at an amino acid residue site selected from the group consisting of: 283, 363, 394 and 463 of SEQ ID NO. 2.

20. (Previously presented) The DNA according to claim 5, wherein the DNA comprises a member selected from the group consisting of

(a) the DNA of SEQ ID Nos 4, 8, 12 and 16, said DNA comprising a mutated phosphorylation site,

(b) a DNA hybridizing with the DNA from (a) under high stringency conditions, said DNA comprising the mutated phosphorylation site of the DNA from (a), or

(c) a DNA related to the DNA from (a) or (b) via the degenerated genetic code.

21. (Previously presented) A parvovirus NS I variant protein having a shifted equilibrium between the DNA replication and transcription activities (a) and the cytotoxicity activity (b), wherein the parvovirus NS 1 variant protein comprises a mutated phosphorylation site and wherein the shifted equilibrium is selected from the group consisting of

(1) DNA replication activity is reduced, transcription activity is eliminated and cytotoxicity is maintained or increased; and

(2) DNA replication activity and transcription activity is maintained or increased and cytotoxicity is reduced or eliminated.

22 (New) The parvovirus NS1 variant protein according to claim 1, wherein the protein comprises SEQ ID NO:6, SEQ ID NO: 10, SEQ ID NO: 14, or SEQ ID NO: 18.